Modern Concepts of Cardiovascular Disease

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THE INFLUENCE OF EXTRINSIC FACTORS ON THE CORONARY SYSTEM

Both the normal and the abnormal heart are constantly under the influence of stimuli carried to them by the autonomic nervous system. Normally, such stimuli keep in perfect balance the heart and the ever-changing needs of the body for blood supply. They influence also in part the intrinsic blood supply to the heart muscle itself. Well organized as is the autonomic control, reflexes occasionally occur which are not normal, and which are not to the advantage of the heart or the organism which it serves. Just why this should be, we can not speculate upon at any length. Many of those in whom these apparently purposeless reflexes occur, belong to the group who have what Houston terms a "spasmogenic aptitude." It is possible, also, that there is a lack of some higher inhibition and control of reflexes. In the experimental animal such reflexes as we have dealt with here are much more readily obtained in the decerebrate animal which is free from such higher inhibition. It is possible, also, that as Lewis points out in regard to vagal heart block, there may be tissue changes which predispose to such reflex action.

In heart disease, and especially in angina pectoris, conditions occur which are difficult to explain on the basis of anatomic changes in the heart or its vessels alone. The relationship between sclerosed and narrowed coronary vessels and anginal pain is obvious and well established. This is the one major factor. Other anatomical changes in the heart and the great vessel are also valent. On the other hand, we frequently see cases which we find difficult to explain on the basis of pathological changes alone.

Even in patients in whom we can confidently assume definite pathological changes in the heart or in the coronary vessels, the occurrence of anginal attacks or of other conditions may be influenced by such extrinsic factors as the time relation to meals, the inspiration of cold air through the nostrils or other conditions.

The occurrence of anginal pain "more particularly when they walk soon after eating" was mentioned by Heberden, and has been mentioned by most other writers since his time. Anginal pain after meals may occur when sitting quietly. One reason for the occurrence of anginal pain after meals is probably concerned with the increased work demanded of the heart during the period of digestion. But this would not explain why such attacks are not a constant phenomenon in the same patient after comparable meals and under similar conditions. It is a frequent experience, also, to have the pain disappear immediately when gas is expelled from the stomach.

von Bergmann and his associates did a great deal to explain the increased frequency of anginal pain after meals, when they demonstrated in the experimental animal that there was a marked decrease in coronary flow when the stomach was distended by means of a balloon placed within it. That this was due to a reflex vasoconstriction of the coronary vessels was indicated by the fact that this decrease in coronary flow did not occur after the vagi were cut, or after atropine was administered. The response was more readily elicited if the bag was inflated at the cardiac end of the stomach at the aesophageal hiatus. Similar results were obtained by distention of the aesophagus.

Dr. Fenn, Dr. LeRoy and I repeated this work upon the stomach with identical results. Dr. LeRoy was also able to show that it occurred in the unanesthetized animal which was carrying a Rein thermo-stromuhr. We showed also that the same decrease in coronary flow occurred when the free abdominal cavity was distended with air. Again, this did not occur after atropine or after the vagi were sectioned. Clinically anginal pain is seen to occur when the abdomen is distended with gas, and to be relieved by the expulsion of flatus. It is to be noted, however, that in some cases this is associated with a hiatus hernia, which is reduced when the intra-abdominal pressure is relieved. There is also the possibility of a reflex from the bowel itself.

Clinical experiments confirm the work upon animals. If we ask a patient subject to angina of effort to breathe a mixture of air low in oxygen content, anginal pain occurs after so many minutes, relieved at once when a valve is turned which substitutes pure oxygen. If the experiment is repeated after a meal during the period of digestion, pain comes on much sooner than when it is performed upon an empty stomach. The pain does not come on sooner if atropine is administered before the ingestion of the meal.

When von Bergmann performed his experiments upon animals, he found a more marked effect upon coronary flow if the bag were distended at the aesophageal hiatus. Clinically, hiatus hernia is frequently associated with anginal pain and the attacks become less frequent or disappear when steps are taken to relieve the hiatus hernia. The attacks are frequently connected with events which cause or accentuate the hernia, as bending over, coughing, lifting, or any movement which increases intra-abdominal pressure. The anginal pain may occur on assuming a recumbent position, especially after

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meals, and be relieved by standing up. Electrocardiographic changes indicative of coronary involvement may appear when the hernia is present, and disappear when it is reduced.

Diverticula of the aesophagus are another frequent source of anginal pain, and von Bergmann demonstrated the reflex character of this pain. Diverticula of the duodenum are frequently associated with anginal pain. The association of duodenal ulcer is very frequently noted.

The association of anginal pain with gall bladder disease has been commented upon frequently since Babcock's early observation. Clinical and electrocardiographic evidence was presented by Schwartz and Herman, Fitzhugh, and others. Fenn, LeRoy and I found the coronary flow to be decreased in the experimental animal upon distention of the gall bladder or the cystic duct, although the evidence was not altogether conclusive. Recently, MacArthur and Wakefield, in some as yet unpublished work, have shown that electrocardiographic changes, such as depression of the T Wave in Lead 2, prolongation of the P-R interval, and premature ventricular contractions, occur during the course of gall bladder operations when the gall bladder is distended with normal saline solution or traction made upon it.

Danielopolu was the first to suggest that anginal pain might occur reflexly from stimuli originating in the thoracic cavity. Scherf and Schonbrunner observed that lung emboli were associated with anginal pain, and that the vagus was involved, was indicated by Kaufman who observed a case of heart block associated with lung embolus. deTakats, Beck, and Fenn observed electrocardiographic changes following lung emboli similar to those observed in coronary occlusion, and in the experimental animal showed the changes to be due to a vagal reflex. deTakats and Jesser showed a marked decrease in mortality when atropine, with either papaverine or aminophyllin, was administered immediately.

A patient will very frequently state that his anginal attacks are brought on by breathing cold air through the nose, or facing a cold wind. He may have found out for himself that this may be avoided by holding a muffler or handkerchief over his nose and breathing through his mouth. Pulmonary edema may also be similarly precipitated.

Dogiel, as far back as 1866, showed that a reflex slowing of the pulse occurred when the nasal mucus membrane was stimulated. This was confirmed by many others, who showed that the reflex persisted in a less marked degree, after vagal section or atropine. von Skramlick, in his summary of the work upon this reflex, states that stimulation of the nasal mucus membrane not only produces a stimulation of the inhibitory vagus fibers, but also an inhibition of the tonic effect of the sympathetic fibers. When Fenn, Le Roy, and I repeated the work upon the dog, but, in addition, measured the coronary flow with either a Morovitz cannula or a Rein thermo-stromuhr, not only was a decrease of pulse rate and rise in blood pressure observed, but there was a definite decrease in coronary flow. These changes persisted after atropine or vagal section. If a sympathetic stimulator, such as ergotamine tartrate was used, the same results occurred.

When a patient subject to attacks of angina of effort was allowed to breathe an oxygen-poor mixture, anginal pain occurred much sooner after ergotamine tartrate than it did in the control experiments where no drug was given. Pain may occur with ergotamine tartrate, even without breathing the air low in oxygen content. As Katz had pointed out, this may be due to the direct vascoconstricting effect of the drug upon vessel walls. But whatever the mechanism, it is just as well to remember that it may occur.

The reflex vascoconstriction of the other remaining coronary vessels of the heart when one vessel is occluded, is of very great importance, as it has very immediate bearing upon the mortality in coronary occlusion, as well as on the after effects. This reflex was demonstrated in the Banting Laboratory by Manning, Hall and McEachern. They showed in the experimental animal that if one coronary artery were occluded, there was a reflex vascoconstriction of the uninvolved arteries, decreasing the blood supply to the uninfarcted heart muscle, and decreasing the flow to the infarcted heart muscle through the anastomosing vessels. If the vagi are cut, or atropine administered, or both stellate ganglia and the upper five thoracic ganglia are removed, this does not occur, and the same very low mortality results as when an artery is occluded under full anesthesia. To further demonstrate that this was due to reflex action, and not to a fall in blood pressure, they measured the flow in an unobstructed artery when another artery was ligated. The flow in the unobstructed artery was reduced. But if the stellate ganglia were removed, this did not occur.

LeRoy repeated the work with similar results. In the case of dogs, the mortality was not only reduced by the use of atropine, but was still further reduced if theobromine sodium acetate was administered at the same time.

There is clinical evidence to indicate that by keeping the results of the experimental work in mind, and administering atropine subcutaneously immediately after a coronary occlusion has occurred, the mortality will be materially reduced. It will be further reduced if a coronary vasodilator drug such as aminophyllin or papaverin is used with the atropine. It can be assumed that if the flow in the anastomosing vessels is improved, the infarct will be smaller and the endocardium less extensively involved, with less chance of mural thrombi and resulting emboli.

At times, anginal pain occurs when the blood pressure rises temporarily to levels which are much higher than normal for the individual. This is not entirely due to increased work of the heart. Anrep has shown in the experimental animal that when the intra-cephalic pressure is increased in the animal there is a reflex decrease in coronary flow mediated through the vagus. Clinically, anginal pain may occur with sudden increases in blood pressure, relieved by the vasodilator action of nitroglycerine, even though the blood pressure may not fall.

What has been said here concerns itself altogether with the coronary flow. Reflex changes in the heart rate, and the effect of the vagus in inducing heart block are too well known to merit comment. There are doutbless other reflex effects which have not been explained and which can only be surmised at present.

Note: Most of this material appeared previously in the Bulletin of the New York Academy of Medicine, 1942 18 83, where full references are given.

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